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3D reconstruction of BigBrain2: Progress report on updated processing pipeline and application to existing annotations and cortical surfaces

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The development of BigBrain2 is a continuation of the first BigBrain [1] that will contribute new insight on inter-subject cytoarchitectonic variability. Overall, BigBrain2 offers better quality staining, favorable to regional segmentation and registration, and contains fewer artefacts through sectioning and staining. In this presentation, we will report about the initial 3D reconstruction of BigBrain2 at 100µm, which is suitable already for the extraction of cortical surfaces and the representation of annotations of some cortical and subcortical regions.

The paraffin embedded fixed brain of a 30-year-old male donor was sectioned coronally at 20µm thickness using a large-scale microtome. All 7676 sections were stained for cell bodies (Merker stain), then scanned at 10µm in-plane (flatbed scanner, 8bit grey level encoding) and subsequently at 1µm in-plane (Huron TissueScope scanner). The histological flatbed scanner sections were resampled at 20µm in-plane, to match the section thickness, and manual and semi-automatic corrections were performed to repair acquisition artifacts due to sectioning and histological preparation (tears, folds, missing tissue, excessive distortion etc.) [2]. Every fifth section was initially repaired, with comprehensive quality control (QC), from which a first 3D reconstruction was obtained at an effective section spacing of 100µm. Data provenance tracking of all repair operations provides a means for assessing the extents of the repaired artifacts and for eventual reproducibility at the 1µm in-plane resolution. The repaired sections were aligned to the post-mortem MRI of the fixed brain (Siemens Sonata, 1.5T, MPRAGE, 0.5mm) in an iterative process by 3D registration of the stacked images to the MRI, followed by 2D registration of the individual images to the sliced MRI, while gradually increasing the degree of 2D and 3D registration from rigid-body to affine to non-linear across 10 global iterations. These extra global iterations helped resolve the lower-frequency alignment errors causing jaggies. Alignment to the MRI enables to correct for tissue compression caused by cutting and mounting of sections, and tissue shrinkage. Ultimately, section-to-section non-linear 2D alignment (without MRI) was performed to resolve high-frequency alignment errors. Optical-balancing was applied by normalizing image intensities to the MRI data to correct for staining imbalances across the brain. The reconstructed 3D volume is obtained at 100µm in the MRI ex-vivo space, which is suitable for the extraction of cortical surfaces. Finally, computed transformations are saved and can be applied to regions annotated on the original sections.

Ongoing work includes the semi-automatic repairs of the remaining sections (80%) to obtain a complete volume at 20µm isotropic resolution onto which sections at the cellular resolution of 1µm can be progressively overlaid.

References:

[1] Amunts K. et al., BigBrain: An Ultrahigh-Resolution 3D Human Brain Model. Science, 2013.

[2] Mohlberg H. et al., 3D reconstruction of BigBrain2: Challenges, methods, and status of histological section repair –A progress report. BigBrain Workshop 2022

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